

Combination Chemotherapy With Carboplatin and Bleomycin for Advanced and Recurrent Head and Neck Cancer: A Phase II Study

JOSE L. GONZALEZ-VELA, MD, LAWRENCE PANASCI, MD, MARTIN BLACK, MD,
MICHAEL POLLAK, MD, AND RICHARD MARGOLESE, MD

*From the Oncology and Otorhinolaryngology Departments, Jewish General Hospital,
McGill University, Montreal, Quebec, Canada*

Carboplatin is a platinum analogue with activity reported in head and neck cancer. We conducted a phase II trial with 14 patients who had recurrent head and neck cancer. They were treated with carboplatin 300 mg/m² intravenously (I.V.) and bleomycin 30 units I.V. every 4 weeks. No responses were observed in this group of patients. Dose intensity of carboplatin administration may be an important determinant of response.

KEY WORDS: head and neck cancer, chemotherapy, dose intensity

INTRODUCTION

Despite reports of high response rates with initial chemotherapy for patients with advanced squamous carcinomas of the head and neck, the outlook for this disease has not changed significantly in the past two decades. Drugs including methotrexate, cisplatin, bleomycin, and 5 fluorouracil have been reported to be active [1]. Combinations of these drugs have resulted in high response rates, but their impact on survival is not certain [2]. Carboplatin, a cisplatin analogue, has recently been shown to be active as a single agent with approximately a 25% response rate [3]. We conducted a clinical trial to assess the response rate and toxicity of carboplatin and bleomycin in patients with recurrent or advanced head and neck cancer.

MATERIALS AND METHODS

Between January 1986 and February 1987, 14 patients with recurrent or advanced squamous carcinoma of the head and neck received carboplatin 300 mg/m² of body surface area intravenously (I.V.) and bleomycin 30 units every 4 weeks. Pretreatment studies included a history, physical examination, CBC, liver function tests, and a chest x-ray. Computerized tomograms of the head and neck, laryngograms, and other special studies were performed when considered useful for assessing response or pretreatment staging. We obtained a CBC and blood chemistries prior to each treatment, and the patients were evaluated for response by two examiners. All patients

were previously treated with radiotherapy and/or surgery. Only one of the patients received prior chemotherapy with trimetrexate and had a partial response to that agent before progressing. We defined 1) complete response as disappearance of all clinical evidence of tumor; 2) partial response as 50% decrease in the sum of the products of perpendicular diameters of measured lesions without increase in the size of any lesion or the appearance of new lesions; 3) stable disease as less than 50% decrease in measurable lesions or less than 25% increase in any lesion; 4) progressive disease as more or equal to 25% increase in any lesion or the appearance of new lesions. Toxicity was reported according to the World Health Organization for acute and subacute toxicity [4].

RESULTS

Table I shows the patient characteristics. Most patients had an ECOG performance status of 2 and local regional recurrent disease. All patients received a minimum of one and a maximum of four cycles of chemotherapy (the mean number of cycles was 2). We observed three episodes of hematologic toxicity; two were grade II, and one was grade III. The grade III toxicity was observed after the fourth cycle of chemotherapy; grade II toxicity was observed on the preceding cycle in this patient. The

TABLE I. Patient Characteristics

Patient characteristics	
No. entered:	14
Sex (m/f):	9/5
Median age (range): 60 years (47-77)	
ECOG performance scale	
0:	0
1:	3
2:	10
3:	1
4:	0
Primary Site	
Larynx:	4
Hypopharynx:	2
Oral cavity:	7
Nasopharynx:	0
Unknown primary:	1
No. with local/regional disease:	13
No. with distant metastases only:	1
No. with both:	2

other case of grade II toxicity was observed in the only patient who had received prior chemotherapy. Six patients experienced grade I nausea, and one patient had grade IV toxicity with intractable nausea for 1 week. We did not observe any measurable response, complete or partial, in any of the 14 patients. Mean survival from the 1st day of treatment with chemotherapy was 3 months, with a range from 1 to 5 months.

DISCUSSION

Carboplatin has been reported to be an active drug in squamous cancer of the head and neck, as has bleomycin. The disappointing result of this study may well be related to the dosages used, which were lower than those employed in single-agent studies.

CONCLUSIONS

This dosage and schedule of carboplatin and bleomycin results in moderate hematologic and gastrointestinal toxicity, which was mostly well tolerated. The response rate is probably less than 20%, but there is a possibility that the dose intensity of carboplatin may be an important determinant of response.

REFERENCES

1. Bertino JR, Moshier MB, De Conti RC: Chemotherapy of cancer of the head and neck. *Cancer* 31:1141-1149, 1973.
2. Vogel SE, Schoenfield DA, Kaplan BH, Lerner HJ, Engstrom PF, Horton J: A randomized prospective comparison of methotrexate with a combination of methotrexate, bleomycin, and cisplatin in head and neck cancer. *Cancer* 56:432-442, 1985.
3. Eisenberger M, Hornedo J, Silva H, Donehower R, Spaulding M, Van Echo D: Carboplatin (NSC-211-140): An active platinum analogue for the treatment of squamous cell carcinoma of the head and neck. *J Clin Oncol* 4:1506-1509, 1986.
4. Miller AB, Hoogstraten B, Staquet M, Winkler A: Reporting results of cancer treatment. *Cancer* 47:207-214, 1981.